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Society for Maternal-Fetal Medicine Consult Series #69: Hepatitis B in pregnancy: updated guidelines

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The American College of Obstetricians and Gynecologists (ACOG) endorses this document.

More than 290 million people worldwide, and almost 2 million people in the United States, are infected with hepatitis B virus, which can lead to chronic hepatitis B, a vaccine-preventable communicable disease. The prevalence of chronic hepatitis B infection in pregnancy is estimated to be 0.7% to 0.9% in the United States, with >25,000 infants born annually at risk for chronic infection due to perinatal transmission. Given the burden of disease associated with chronic hepatitis B infection, recent national guidance has expanded both the indications for screening for hepatitis B infection and immunity and the indications for vaccination. The purpose of this document is to aid clinicians caring for pregnant patients in screening for hepatitis B infection and immunity status, discuss the perinatal risks of hepatitis B infection in pregnancy, determine whether treatment is indicated for maternal or perinatal indications, and recommend hepatitis B vaccination among susceptible patients. The following are the Society for Maternal-Fetal Medicine recommendations: (1) we recommend triple-panel testing (hepatitis B surface antigen screening, antibody to hepatitis B surface antigen, and total antibody to hepatitis B core antigen) at the initial prenatal visit if not previously documented or known to have been performed (GRADE 1C); (2) we recommend universal hepatitis B surface antigen screening alone at the initial prenatal care visit for all pregnancies where there has been a previously documented negative triple-panel test (GRADE 1B); (3) we recommend that individuals with unknown hepatitis B surface antigen screening status be tested on any presentation for care in pregnancy; we also recommend that those with clinical hepatitis or those with risk factors for acute hepatitis B infection be tested at the time of admission to a birthing facility when delivery is anticipated (GRADE 1B); (4) we do not recommend altering routine intrapartum care in individuals chronically infected with hepatitis B; administration of neonatal immunoprophylaxis is standard of care in these situations (GRADE 1B); (5) we do not recommend cesarean delivery for the sole indication of reducing perinatal hepatitis B virus transmission (GRADE 1B); (6) we recommend that individuals with HBV infection can breastfeed as long as the infant has received immunoprophylaxis at birth (GRADE 1C); (7) we suggest individuals with hepatitis B infection who desire invasive testing may have the procedure performed after an informed discussion on risks and benefits in the context of shared decision-making and in the context of how testing will affect clinical care (GRADE 2C); (8) in individuals with hepatitis viral loads >200,000 IU/mL (>5.3 log 10 IU/mL), we recommend antiretroviral therapy with tenofovir (tenofovir alafenamide at 25 mg daily or tenofovir disoproxil fumarate at 300 mg daily) in the third trimester (initiated at 28–32 weeks of gestation) as an adjunctive strategy to immunoprophylaxis to reduce perinatal transmission (GRADE 1B); (9) we recommend administering hepatitis B vaccine and hepatitis B immunoglobin within 12 hours of birth to all newborns of hepatitis B surface antigen–positive pregnant patients or those with unknown or undocumented hepatitis B surface antigen status, regardless of whether antiviral therapy has been given during the pregnancy to the pregnant patient (GRADE 1B); and (10) we recommend hepatitis B vaccination in pregnancy for all individuals without serologic evidence of immunity or documented history of vaccination (GRADE 1C).

Key words: antiviral therapy, breastfeeding, chronic hepatitis B, immunoprophylaxis, intrapartum care, neonatal care, perinatal transmission, viral load

Introduction

Between 800,000 and 1.8 million people in the United States and >290 million people worldwide are infected with hepatitis B virus (HBV), which can lead to hepatitis B, a vaccine-preventable communicable disease.[1–4] The estimated prevalence of chronic hepatitis B infection among pregnant women in the United States is 0.7% to 0.9%,[5,6] with >25,000 infants born annually at risk for chronic infection.[7] Although transmission through sexual intercourse and intravenous drug use are major risk factors for acquisition of HBV among adults in the United States, perinatal transmission is responsible for up to 50% of HBV infections worldwide. Approximately two-thirds of people with hepatitis B are unaware of their infection.[3,8,9] The risks of acquiring hepatitis B may be unrecognized. Updated recommendations call for universal hepatitis B screening during pregnancy and in adults aged ≥18 years, and universal vaccination through the age of 59 years, given that anyone can be infected with HBV.[4,10]

In contrast to HBV acquisition in adulthood, which more commonly leads to resolution of acute infection and lifelong immunity, perinatal HBV is more likely to lead to chronic infection and associated long-term sequelae. Chronic hepatitis B infection will develop in up to 90% of perinatally exposed neonates who do not receive appropriate immunoprophylaxis, in contrast to 10% to 25% of infected children and 5% to 10% of exposed immunocompetent adults. Among all individuals with chronic HBV infection, regardless of the timing of infection, 20% will eventually die of complications of HBV infection, including cirrhosis, end-stage liver disease, and hepatocellular carcinoma.[11] Chronic HBV infection is the major source of hepatocellular carcinoma globally, leading to 50% of cases worldwide and 80% of cases in high-endemic areas. An estimated 2.4 million people in the United States have chronic hepatitis B, with persons of Asian or African descent being disproportionately affected.[2] Rates of acute hepatitis B are known to vary by race and ethnicity. In 2021, reported rates ranged from 0.2 cases per 100,000 among non-Hispanic Asian/Pacific Islander persons to 0.9 cases in non-Hispanic Black persons. Rates of infection increased in 2021 among non-Hispanic Black and Hispanic persons.[12] It is unclear if these racial discrepancies are due to differences in duration of infection, hepatitis B genotypes, varied access to care and treatment, or social determinants of health.

The purpose of this document is to aid clinicians caring for pregnant patients in screening for hepatitis B infection and immunity status, discuss the risks of perinatal hepatitis B transmission, determine whether treatment is indicated for maternal or perinatal indications, and recommend hepatitis B vaccination among susceptible patients.

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What are the recommendations for hepatitis B virus screening for infection and immunity in pregnancy?

Universal screening for hepatitis B infection with hepatitis B surface antigen (HBsAg) during each pregnancy at the first prenatal visit is cost-effective[13] and recommended by the American College of Obstetricians and Gynecologists (ACOG) and the United States Preventive Services Task Force (Grade 1A).[14–16] In March 2023, the Centers for Disease Control and Prevention (CDC) expanded screening recommendations to include a universal *triple-panel screen* (HBsAg, antibody to HBsAg [anti-HBs], and total antibody to hepatitis B core antigen [total anti-HBc]) in all adults at least once in their adult lifetime.[10] The purpose of this comprehensive testing approach is to fully characterize whether an individual is immune because of infection, immune because of vaccination, infected with HBV, or susceptible to HBV infection. Universal one-time triple-panel testing regardless of vaccination status helps identify those who are still susceptible to infection and screens those with ongoing risk without relying on risk-based screening. Details on interpreting test results are included in Table 1. HBsAg and anti-HBc only develop after natural infection, whereas anti-HBs can develop after infection or immunization. Early detection of HBV can reduce morbidity, mortality, and perinatal transmission.[17–19] **We recommend triple-panel testing (HBsAg, anti-HBs, and total anti-HBc) at the initial prenatal visit if not previously documented or known to have been performed (GRADE 1C). We recommend universal HBsAg screening alone at the initial prenatal care visit for all pregnancies where there has been a previously documented negative triple-panel test (GRADE 1B).** The triple panel can also be performed at a prepregnancy visit, if not previously performed in the individual's adult life, to further inform a patient's potential for HBV acquisition in pregnancy and need for vaccination. This recommendation is in line with the CDC and ACOG recommendations to identify not only those infected with HBV but also those who are immune and susceptible.[10,14]

Testing individuals of unknown HBsAg status can identify neonates in need of HBV immunoprophylaxis to reduce the risk of perinatal transmission[17,18,20] (see "What is the neonatal management of infants born to individuals with chronic HBV infection?"). **We recommend that individuals with unknown HBsAg status be tested on any presentation for care in pregnancy. We also recommend that those with clinical hepatitis or those with risk factors for acute hepatitis B infection be tested at the time of admission to a birthing facility when delivery is anticipated (GRADE 1B).**[10,14,16,19]

What are the obstetrical implications of pregnancies complicated by chronic hepatitis B infection?

With the exception of the lifelong implications of perinatal HBV infection, data are insufficient to suggest that acute or

TABLE 1
Interpretation of hepatitis B serologic test results[21]

Triple-panel laboratory results					
Hepatitis B surface antigen (HBsAg)	**Hepatitis B surface antibody (anti-HBs)**	**Hepatitis B core antibody (anti-HBc)**	**Hepatitis B status interpretation**	**Management**	**Vaccination**
Negative	Negative	Negative	Susceptible	None	Recommended
Positive	Negative	Positive	Hepatitis B infection	Evaluation for treatment in pregnancy[a] Refer to hepatitis/infectious diseases care	Not recommended
Negative	Positive	Positive	Immune, due to previous infection	If immunocompetent: none If immunocompromised: refer to hepatitis/infectious diseases care	Not recommended
Negative	Positive	Negative	Immune, due to vaccination	None	Not recommended if documented complete vaccine series; if no documentation, then recommend vaccination
Negative	Negative	Positive	Uncertain[b]	Refer to hepatitis/infectious diseases care	Consider, after hepatitis/infectious diseases evaluation

[a] See section: "Medical management of chronic HBV during pregnancy;"; [b] These serologic results can indicate resolved past infection with waning anti-HBs levels (most common), false-positive total anti-HBc, occult infection, or mutant HBsAg strain not detectable by laboratory assay.

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chronic HBV infection is associated with adverse pregnancy outcomes such as preterm birth, low birthweight, or gestational diabetes. Therefore, routine prenatal care and fetal surveillance are recommended for individuals with chronic HBV infection. Optimal maternal medical management is discussed later (see "What is the medical management of chronic HBV during pregnancy?").

Perinatal HBV transmission can occur prenatally during pregnancy, during labor through contact with infected vaginal blood and secretions, and postnatally through close contact. Procedures during labor and delivery, such as internal monitoring, episiotomy, and operative vaginal delivery, may theoretically increase the risk of transmission. However, neonatal HBV immunoprophylaxis (see "What is the neonatal management of infants born to individuals with chronic HBV infection?") greatly decreases these risks.[20,22,23] Thus, **we do not recommend altering routine intrapartum care in individuals chronically infected with hepatitis B. Administration of neonatal immunoprophylaxis is standard of care in these situations (GRADE 1B).** Planned cesarean delivery has also been discussed as a method of reducing perinatal transmission, but it is not recommended because available data are conflicting and of poor quality.[14,24–28] For example, 2 systematic reviews found that elective cesarean delivery was effective in preventing mother-to-child transmission of HBV; however, the studies used to reach this conclusion were all rated as having moderate to high risk of bias and were relatively low-quality studies.[25,26] Thus, **we suggest individuals with hepatitis B infection who desire invasive testing may have the procedure performed after an informed discussion on risks and benefits in the context of shared decision-making and in the context of how testing will affect clinical care (GRADE 1B).** Similarly, in the setting of neonatal HBV immunoprophylaxis, breastfeeding is not contraindicated.[24,29] Studies have documented no difference in rates of infection between breastfed and formula-fed infants born to HBV-infected women who received immunoprophylaxis, with rates between 0% and 5% in both groups.[30,31] **We recommend that individuals with HBV infection can breastfeed as long as the infant has received immunoprophylaxis at birth (GRADE 1C).** If a breastfeeding individual has bleeding nipples, discard milk from the affected breast while continuing to feed or pump from the unaffected breast until the nipple is healed to prevent direct exposure to blood.

Concerns have also been raised regarding diagnostic procedures during pregnancy, including chorionic villus sampling, amniocentesis, or percutaneous umbilical blood sampling in patients with hepatitis B. Many earlier series did not demonstrate an increased risk of in utero HBV transmission after amniocentesis in women with chronic HBV infection.[32–36] These series were conducted before the routine use of HBV viral load testing as a disease marker and may not apply to individuals with high viral loads. One series did demonstrate an increase in risk for in utero infection after amniocentesis in women with HBV DNA levels (viral loads) >7 log 10 copies/mL compared with women with viral loads below that cutoff (50% vs 4%; odds ratio, 21.3; $P<.006$).[37] Such emerging data may impact counseling surrounding invasive prenatal testing as data accumulate from more

series with information regarding maternal HBV viral load. **We suggest individuals with hepatitis B infection who desire invasive testing may have the procedure performed after an informed discussion on risks and benefits in the context of shared decision-making and in the context of how testing will affect clinical care (GRADE 2C).**[14,24]

Pregnant individuals with chronic HBV infection should be evaluated for immunity to hepatitis A virus and be vaccinated if susceptible. Vaccination for hepatitis A during pregnancy is safe.[38] The Advisory Committee on Immunization Practices (ACIP)-recommended hepatitis A vaccines in pregnancy include the 2-dose vaccines HAVRIX (GlaxoSmithKline) and VAQTA (Merck). In addition, TWINRIX (GlaxoSmithKline) is a combination hepatitis A and B vaccine that can be given in pregnancy. Pregnant individuals should be counseled regarding exposures to potentially hepatotoxic medications, including acetaminophen, and avoiding the use of alcohol even after pregnancy. Individuals should also be counseled that their household contacts should be evaluated for their HBV status and immunized if susceptible. In addition to transmission via exposure to blood and sexual contact, HBV can also be transmitted through shared use of household items (e.g., eating utensils, toothbrushes) and close personal contact; thus, safe, hygienic practices should be applied.

What is the recommended medical management of chronic hepatitis B during pregnancy?

Once chronic hepatitis B infection is identified, baseline liver function tests, HBV DNA levels, and hepatitis B e antigen (HBeAg) are indicated unless recently evaluated by the patient's infectious disease or hepatology provider. HBV DNA levels may be reported in many units; Table 2 lists the typical cutoffs for therapy and conversions between units. Treatment indications for maternal health are based on the presence or absence of cirrhosis, HBV DNA levels, ALT levels, and the presence or absence of HBeAg (Table 2). A referral to infectious disease or hepatology is indicated for patients not already established in care. HBV viral load has been shown to be directly related to the risk of disease progression in nonpregnant adults. In a large prospective cohort from Taiwan, an HBV-DNA level >4 log 10 copies/mL (or >1785 IU/mL) was associated with significantly higher rates of cirrhosis, hepatocellular carcinoma, and death, independently of HBeAg status as a surrogate marker of viremia.[39,40]

Table 2 includes the common treatment thresholds for patients with chronic hepatitis B but does not include every possible scenario, such as the influence of liver biopsy findings on treatment thresholds.

The American Association for the Study of Liver Diseases issued revised guidelines[41] in 2018 for the treatment of chronic HBV infection, with tenofovir as a first-line therapy. Lamivudine is no longer a first-line agent because of resistance concerns.[42] More recent reports have demonstrated that in chronically infected adults, tenofovir monotherapy has maintained HBV-DNA suppression while used for up to 6 years of continuous treatment, with no evidence of tenofovir resistance, even in patients whose virus became resistant to lamivudine.[44,45] Recently, a new formulation of tenofovir, tenofovir alafenamide fumarate (TAF), has been approved for the treatment of chronic hepatitis B, as it has lower risks of affecting bone density and renal function with long-term use compared with the traditional formulation, tenofovir disoproxil fumarate (TDF). Data on TAF use in pregnancy mostly arise from observational studies in pregnant women with HIV and chronic hepatitis B. No safety signals have been identified in the reported data, with efficacy noted in preventing perinatal transmission.[46–50] TAF-containing regimens are currently first-line therapy among pregnant individuals with HIV.[51]

Repeated liver function tests and HBV DNA level measurements should be performed in the early third trimester (28–32 weeks of gestation) among individuals without a maternal indication for treatment. Maternal HBV-DNA levels have been demonstrated to be the strongest predictor of neonatal immunoprophylaxis failure, with an inverse correlation between maternal viral load and immunoprophylaxis efficacy. Earlier studies showed an effective prophylaxis rate close to 100% if prelabor HBV-

TABLE 2
Common indications for hepatitis B treatment in pregnancy, stratified by hepatitis B virus DNA thresholds and maternal vs perinatal indications, in individuals without cirrhosis

HBV DNA level	Treatment thresholds for maternal health	Treatment threshold for perinatal transmission prevention
IU/mL	eAg negative: >2000 and ALT >2× ULN eAg positive: >20,000 and ALT >2× ULN	>200,000
Log 10 IU/mL	eAg negative: >3.3 log 10 IU/mL and ALT >2× ULN eAg positive: >4.3 log 10 IU/mL and ALT >2× ULN	>5.3 log 10 IU/mL
Log 10 copies/mL	eAg negative: >4.0 log 10 copies/mL and ALT >2× ULN eAg positive: >5.0 log 10 copies/mL and ALT >2× ULN	>6.0 log 10 copies/mL

The World Health Organization has recommended that HBV DNA be expressed in terms of IU/mL. Conversion between units is as follows: to convert from IU/mL to copies/mL, the IU/mL value should be multiplied by 5.6 (or the copies/mL value similarly divided).[43]

eAg, hepatitis B e antigen; *HBV*, hepatitis B virus; *ULN*, upper limit of normal.

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Summary of recommendations

Number	Recommendation	Grade
1	We recommend triple-panel testing (HBsAg, antibody to HBsAg [anti-HBs], and total antibody to hepatitis B core antigen [total anti-HBc]) at the initial prenatal visit if not previously documented or known to have been performed.	1C
2	We recommend universal HBsAg screening alone at the initial prenatal care visit for all pregnancies where there has been a previously documented negative triple-panel test.	1B
3	We recommend that individuals with unknown HBsAg status be tested on any presentation for care in pregnancy. We also recommend that those with clinical hepatitis or those with risk factors for acute hepatitis B infection be tested at the time of admission to a birthing facility when delivery is anticipated.	1B
4	We do not recommend altering routine intrapartum care in individuals chronically infected with hepatitis B. Administration of neonatal immunoprophylaxis is standard of care in these situations.	1B
5	We do not recommend cesarean delivery for the sole indication of reducing perinatal HBV transmission.	1B
6	We recommend that individuals with HBV infection breastfeed as long as the infant receives immunoprophylaxis at birth.	1C
7	We suggest individuals with hepatitis B infection who desire invasive testing may have the procedure performed after an informed discussion on risks and benefits in the context of shared decision-making and in the context of how testing will affect clinical care.	2C
8	In individuals with hepatitis B viral loads >200,000 IU/mL (>5.3 log 10 IU/mL), we recommend antiviral therapy with tenofovir (TAF at 25 mg daily or TDF at 300 mg daily) in the third trimester (initiated at 28–32 weeks of gestation) as an adjunctive strategy to immunoprophylaxis to reduce perinatal transmission.	1B
9	We recommend administering hepatitis B vaccine and HBIG within 12 hours of birth to all newborns of HBsAg-positive pregnant patients or those with unknown or undocumented HBsAg status, regardless of whether antiviral therapy has been given during the pregnancy to the pregnant patient.	1B
10	We recommend hepatitis B vaccination in pregnancy for all individuals without serologic evidence of immunity or documented history of vaccination.	1C

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DNA levels were <5.5 log 10 copies/mL (<4.8 log 10 IU/mL),[52,53] with prospective studies showing a stepwise decrease in prophylaxis effective rate as HBV-DNA levels increased above 6 to 8 log 10 copies/mL (equivalent to 5.3–7.3 log 10 IU/mL).[54,55] A maternal HBV-DNA level >200,000 IU/mL (>5.3 log 10 IU/mL) at delivery appears to be the most important predictor of in utero mother-to-child transmission and prophylaxis failure.[56] A recent systematic review and meta-analysis on the efficacy and safety of antiviral prophylaxis during pregnancy to prevent perinatal hepatitis B infection found that maternal antiviral prophylaxis is highly effective[57] in combination with neonatal immunoprophylaxis, with a pooled odds ratio for transmission of 0.10 (95% confidence interval, 0.03–0.35) for TDF across 19 studies. In addition, maternal antiviral therapy was not found to increase the risks of any infant or maternal safety outcomes. Perinatal antiviral prophylaxis is also cost-effective across a wide range of assumptions.[58]

In individuals with hepatitis B viral loads >200,000 IU/mL (>5.3 log 10 IU/mL), we recommend antiviral therapy with tenofovir (TAF at 25 mg daily or TDF at 300 mg daily) in the third trimester (initiated at 28–32 weeks of gestation) as an adjunctive strategy to immunoprophylaxis to reduce perinatal transmission (GRADE 1B).[14] Individuals with hepatitis B viral loads <200,000 should not start using tenofovir because immunoprophylaxis is highly effective in preventing perinatal transmission with lower viral loads.[41] In addition, tenofovir can have adverse effects, and hepatitis B infection can worsen when tenofovir is stopped.

Pregnant individuals using TAF before pregnancy should continue TAF throughout the pregnancy. Among pregnant individuals initiating tenofovir therapy in pregnancy for maternal health indications, shared decision-making should guide whether to choose TAF or TDF, with a preference for TAF because this agent is more likely to be the patient's long-term therapy. Among pregnant individuals who require tenofovir therapy solely in the third trimester to decrease perinatal transmission risk, either TAF or TDF is appropriate after shared decision-making with the patient.

Discontinuation of antiviral medications after delivery is common for women whose indication for treatment was perinatal transmission prevention. However, discontinuation

Society for Maternal-Fetal Medicine grading system: GRADE (Grading of Recommendations Assessment, Development and Evaluation) recommendations[73,a]

Grade of recommendation	Clarity of risk and benefit	Quality of supporting evidence	Implications
1A. Strong recommendation, high-quality evidence	Benefits clearly outweigh risks and burdens, or vice versa	Consistent evidence from well-performed, randomized controlled trials, or overwhelming evidence of some other form Further research is unlikely to change confidence in the estimate of benefit and risk	Strong recommendation that can apply to most patients in most circumstances without reservation Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present
1B. Strong recommendation, moderate-quality evidence	Benefits clearly outweigh risks and burdens, or vice versa	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design Further research (if performed) is likely to have an impact on confidence in the estimate of benefit and risk and may change the estimate	Strong recommendation that applies to most patients Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present
1C. Strong recommendation, low-quality evidence	Benefits appear to outweigh risks and burdens, or vice versa	Evidence from observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws Any estimate of effect is uncertain	Strong recommendation that applies to most patients Some of the evidence base supporting the recommendation is, however, of low quality
2A. Weak recommendation, high-quality evidence	Benefits closely balanced with risks and burdens	Consistent evidence from well-performed randomized controlled trials or overwhelming evidence of some other form Further research is unlikely to change confidence in the estimate of benefit and risk	Weak recommendation; best action may differ depending on circumstances or patients or societal values
2B. Weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burdens; some uncertainty in the estimates of benefits, risks, and burdens	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design Further research (if performed) is likely to have an effect on confidence in the estimate of benefit and risk and may change the estimate	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances
2C. Weak recommendation, low-quality evidence	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens	Evidence from observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws Any estimate of effect is uncertain	Very weak recommendation, other alternatives may be equally reasonable
Best practice	Recommendation in which either (1) there is an enormous amount of indirect evidence that clearly justifies strong recommendation (direct evidence would be challenging, and inefficient use of time and resources, to bring together and carefully summarize), or (2) recommendation to the contrary would be unethical	—	—

[a] Adapted from Guyatt et al.[74]

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Guidelines

The content of this document reflects the national and international guidelines related to hepatitis B.

Organization	Title	Year of publication
Advisory Committee on Immunization Practices	Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices[19]	2018
Advisory Committee on Immunization Practices	Universal Hepatitis B Vaccination in Adults Aged 19–59 Years: Updated Recommendations of the Advisory Committee on Immunization Practices[65]	2022
American Academy of Pediatrics	Breastfeeding and the Use of Human Milk[29]	2005
American Association for the Study of Liver Diseases	Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance[41]	2017
American College of Obstetricians and Gynecologists	Viral Hepatitis in Pregnancy[14]	2023
Centers for Disease Control and Prevention	Screening and Testing Recommendations for Chronic Hepatitis B Virus Infection (HBV)[10]	2023
Panel on Treatment of HIV During Pregnancy and Prevention of Perinatal Transmission	Recommendations for Use of Antiretroviral Drugs during Pregnancy[51]	2023
Society of Obstetricians and Gynaecologists of Canada	No. 342-Hepatitis B and Pregnancy[24]	2017
United States Preventive Services Task Force	Screening for Hepatitis B Virus Infection in Pregnant Women: US Preventive Services Task Force Reaffirmation Recommendation Statement[16]	2019

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is associated with risks of chronic hepatitis B flare for the first 6 months postpartum, and patients should be counseled on warning signs and have planned laboratory follow-up with their hepatology or infectious disease specialist.[59–61]

What is the neonatal management of infants born to individuals with chronic hepatitis B virus infection?

The mainstay of perinatal HBV infection prevention is a combination of active and passive immunization, known as immunoprophylaxis, for neonates exposed in utero and peripartum, regardless of maternal viral load or maternal antiviral therapy in pregnancy. Before the development of an HBV vaccine, HBV immunoglobulin (HBIG) alone, administered within 12 hours of delivery, was shown to be effective in providing transient passive immunity; however, 25% of infants became infected through household contact by 1 year of age.[62] When the vaccine became available in the 1980s, it was subsequently shown that a combination of HBV vaccine and HBIG given within the first 12 hours after birth provided the greatest degree of durable protection, conferring long-term immunity in 85% to 95% of cases.[22] On-time completion of the full HBV vaccine series following the birth dose is important for the newborn to gain maximal protection. This approach has shown considerable impact on longer-term disease outcome measures for newborns who received prophylaxis in areas where HBV infection is endemic. In Taiwan, the institution of a universal maternal screening and neonatal immunoprophylaxis program lowered the rate of chronic HBV infection among children from 10% to 1% during a 10-year period.[63] Concurrently, the rate of childhood hepatocellular carcinoma was lowered by half in the same population, from 0.7 to 0.36 per 100,000.[64] Immunoprophylaxis is also recommended for infants born to mothers with unknown or undocumented HBsAg status. **We recommend administering the hepatitis B vaccine and HBIG within 12 hours of birth to all newborns of HBsAg-positive pregnant patients or those with unknown or undocumented HBsAg status, regardless of whether antiviral therapy has been given during the pregnancy to the pregnant patient (GRADE 1B).**[14,20]

What is the recommendation for hepatitis B vaccination during pregnancy?

Since April 2022, ACIP has recommended hepatitis B vaccination for all adults aged 19 to 59 years.[65] Hepatitis B immunity in reproductive-age women is not well characterized, but as of 2018, approximately 70% of US adults aged ≥19 years are not fully immunized against hepatitis B.[66] Universal vaccination through the age of 59 years removes the need for risk factor–based screening and thus can increase immunity and decrease hepatitis B incidence, community transmission, and burden of disease.

Hepatitis B vaccination is safe and effective in pregnancy.[67–69] HBV vaccination in pregnancy results in similar seroconversion rates (>90%) to those observed outside of pregnancy, without any vaccine-specific adverse outcomes reported across thousands of pregnancies.[67,68] An accelerated vaccination schedule in pregnancy (0, 1, and 4 months rather than 0, 1, and 6 months) has also been studied, with similar immunogenicity noted.[70] Vaccination series completion rates are also high in pregnancy because of the frequent nature of prenatal care.[71,72] Finally, vaccination in pregnancy is cost-effective, given the lifelong burden of disease that may be avoidable.[13] ACIP-recommended hepatitis B vaccines in pregnancy include the 3-dose vaccines RECOMBIVAX HB (Merck), ENGERIX-B (GlaxoSmithKline), and TWINRIX (GlaxoSmithKline). The 3-antigen hepatitis B vaccine, PreHevbrio (VBI Vaccines), and the 2-dose vaccine, HEPLISAV-B (Dynavax Technologies), have not been studied in pregnancy and thus have insufficient data to inform use in pregnant persons.

Prenatal care may be the earliest opportunity for pregnant adults to interact with a health care provider since the 2022 ACIP recommendations. Given that vaccination is safe and effective in pregnancy, and compliance rates with vaccination are high, prenatal care represents a unique opportunity to complete hepatitis B vaccination during pregnancy. **We recommend hepatitis B vaccination in pregnancy for all individuals without serologic evidence of immunity or documented history of vaccination (GRADE 1C).** Most patients who have documentation demonstrating a completed hepatitis B vaccination series do not need repeated immunization, although there is no evidence that receiving additional doses of the hepatitis B vaccine is harmful.[65] Repeated HBV vaccination might be indicated for health care providers after exposure to HBV; nonresponder infants (infants who did not develop protective surface antibodies after completing 2 full series of the hepatitis B vaccine) born to persons positive for HBsAg; persons on hemodialysis; or immunocompromised persons.[19] In these situations, providers should consult and adhere to the latest CDC guidance. If a patient is unsure of immunity to hepatitis B, and previous triple-panel screening results are unavailable or have never been performed, triple-panel screening is recommended as above. Table 1 outlines interpretation and management of triple-panel testing.

Conclusions

HBV is responsible for a high burden of disease, and perinatally acquired HBV is one of the most common mechanisms of HBV acquisition and development of the chronic carrier state and its sequelae: end-stage liver disease, hepatocellular carcinoma, and cirrhosis. Triple-panel testing once per adult lifetime and HBsAg screening with each pregnancy are intended to optimize perinatal health. These measures allow for universal neonatal immunoprophylaxis and selective maternal antiviral therapy. They also enhance maternal health by identifying susceptible individuals in need of vaccination during pregnancy and individuals in need of infectious disease or hepatology care to prevent the long-term sequelae of hepatitis B. ■

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